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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/562,115	01/19/2006	Yasuhiro Sakurai	126418	1237
25944 7590 03/24/2009 OLIFF & BERRIDGE, PLC P.O. BOX 320850 ALEXANDRIA, VA 22320-4850				
EXAMINER				
O DELL, DAVID K				
ART UNIT		PAPER NUMBER		
1625				
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

### Office Action Summary

**Application No.**

10/562,115

**Applicant(s)**

SAKURAI ET AL.

**Examiner**

David K. O'Dell

**Art Unit**

1625

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 23 December 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-20 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-20 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☒ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SG/US)  
Paper No(s)/Mail Date 5/1/2006
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

**DETAILED ACTION**

1. This application is a 371 of PCT/JP04/09001 filed 06/25/2004 and claims priority to JAPAN 2003-184359 filed 06/27/2003.

**Priority**

2. Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 365(c) as follows:

Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Japan on 6/27/2003. It is noted, however, that applicant has not filed a certified copy of the 2003 application as required by 35 U.S.C. 119(b).

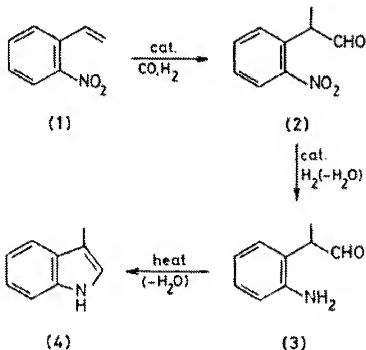
***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1-4, 9-11, are rejected under 35 U.S.C. 102(b) as being anticipated by Ucciani et. al. "Catalytic Synthesis of 3-Substituted Indoles using CO as Building Block and Supported Rhodium as Catalyst." *Journal of the Chemical Society Chemical Communications*, **1981**, 82-83. Ucciani practiced the process of the instant claims where R<sup>2</sup> is a methyl group, n is 0, and R<sup>1</sup> is H (i.e. the conversion of 2 to 4, skatole).



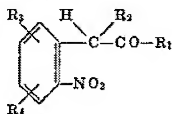
“The expected reaction pathway to skatole can be summarized as in the Scheme, and we wished to discover a method that would lead to highly selective formation of the branched-chain aldehyde (2), and a catalyst which would be able to perform the hydroformylation and nitro-group reduction in one step.”

“Our results indicate the following conclusions. (i) Under severe hydroformylation conditions supported rhodium can act as a reservoir of rhodium carbonyl complexes and as a mass contact able to activate molecular hydrogen, and (ii) a catalytic route to 3-substituted indoles from 2-nitrostyrenes and carbon monoxide is available,”

Of course the conditions of Ucciani et. al. are hydroformylation conditions i.e. (H<sub>2</sub> and CO), however since CO is present in the reaction the instant claims are anticipated.

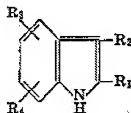
4. Claims 1-3, 7, 8, 9, 10, 13-14, 17, 18 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. 3,682,901. U.S. '901 describes the process of the instant claims at column 1:

Process for preparing 2-substituted indoles (I) by reacting carbon monoxide at elevated temperature and super-atmospheric pressure in the presence of a co-catalyst composition, of which 5% palladium on carbon with a Lewis acid such as ferric chloride is representative, with an o-nitrobenzyl ketone (II):



II

to form:



I

where  $R_1$  is alkyl, aralkyl, aryl or styryl;  $R_2$  is hydrogen, alkyl or aryl, and  $R_3$  and  $R_4$  typically are hydrogen or alkyl.

Several catalysts are mentioned as part of the invention:

The catalyst for the reaction of this invention comprises a noble metal and a Lewis acid as defined in the reference book by Jack Hine, "Physical Organic Chemistry," 1962, McGraw-Hill Book Company, New York. The noble metal may be used either in a metallic or a chemically combined state. It may be employed either with or without a physical support. Among the noble metals which may be employed are platinum, palladium, rhodium, osmium, silver, gold, iridium, and mercury. Palladium is preferred. Among the chemical forms of these metals which can be used are the oxides, sulfates, nitrates and halides, as for example: platinum oxide, rhodium oxide, platinum chloride, rhodium chloride, platinum nitrate, platinum sulfate and the corresponding palladium compounds. The noble metals or compounds thereof may be employed singly or in admixture.

*Claim Rejections – 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

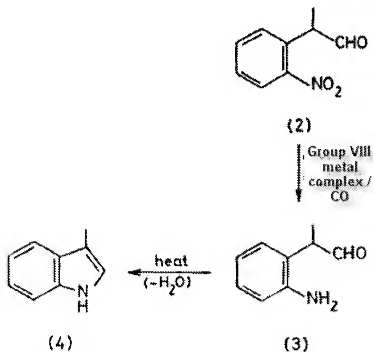
5. Claims 1-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ucciani et. al. "Catalytic Synthesis of 3-Substituted Indoles using CO as Building Block and Supported Rhodium as Catalyst." *Journal of the Chemical Society Chemical Communications*, 1981, 82-83 OR U.S. 3,682,901 AND Sundberg, R.J. *The Chemistry of Indoles*, Academic: 1970, pg 176 AND Cennini et. al. Chapter 5 of CATALYTIC REDUCTIVE CARBONYLATION OF ORGANIC NITRO COMPOUNDS Kluwer: 1997, pgs 177-246 AND Tafesh et. al. "A Review

of the Selective Catalytic Reduction of Aromatic Nitro Compounds into Aromatic Amines, Isocyanates, Carbamates, and Ureas Using CO" *Chemical Reviews* **1996**, 96, 2035-2052.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

- A) Determining the scope and contents of the prior art.
- B) Ascertaining the differences between the prior art and the claims at issue.
- C) Resolving the level of ordinary skill in the pertinent art.
- D) Considering objective evidence present in the application indicating obviousness or nonobviousness.

The instant claims are drawn towards a method of making indoles, in the narrowest embodiment (i.e. where R1 is Me, R2 is H) this is a method making 1-methyl indole, n is 0. As shown below, where R2 is Me, R1 is H:



Sundberg shows that this is a very old reaction, from page 170 “The chemical or catalytic reduction of an *o*-nitrobenzyl ketone generates an *o*-aminobenzyl ketone which can subsequently cyclize and aromatize by dehydration to an indole.” Ucciani et. al. accomplished this reaction with rhodium carbonyl complexes (see the 102 (b) rejection supra). The only claims that are not anticipated (claims 5-8, 12-20) either recite a catalyst other than ruthenium based (claims 5, 12, 16, 20), or amount to a position isomer of the starting material and product of Ucciani (claims 6-8, 13-15, 17-19, where R<sup>1</sup> and R<sup>2</sup> have switched positions). The ‘901 document teaches essentially the same reaction (see the 102 (b) rejection supra), but with Group VIII metals with various lewis acid co-catalysts. Both Cennini and Tafesh teach that a diverse array of group VIII transition metal carbonyl complexes (including Pt and Pd with phosphine ligands) may be used in transformations of this type. The ‘901 document does not mention the catalysts of Tafesh or Cennini because they were not yet known to catalyze this transformation at the time of the ‘901 patent. The presence of the methyl group in either the 1 or 2 position (i.e. starting from the methyl ketone or the aldehyde) will have little consequence on the outcome of the condensation reaction.

According to Tafesh this type of nitro reduction is recognized as industrially important, See conclusions, “The use of CO in the reductive carbonylation of aromatic nitro compounds is very important not only from an academic point of view but also from an industrial one. Its versatility, low cost, and ease of accessibility make it very attractive to the researcher. Its application should find use in the production of agricultural chemicals, pesticides, high performance plastics, polyurethanes, elastomers, and adhesives, and its selective formation of functionalized products can find use in pharmaceuticals as well as the fine chemical industry. It



was found that for each reaction and even for each substrate the catalyst system has to be optimized in view of metal complex, ligand, counterion, and cocatalyst.”

Tafesh also explains that one would choose these reagents over reductants like the metal hydrides, catalytic hydrogenation (or Fe/AcOH as in JP47-38963), in order to avoid potential side reactions, see pg. 2043 “Aromatic amines are important intermediates in the fine chemical, dye, and pigment industry.<sup>87</sup> Aromatic amines are produced by reduction of the corresponding nitro aromatics with a metallo hydride reagent or by catalytic hydrogenation.<sup>88</sup> The selective reduction of nitro aromatic groups in the presence of sensitive functional groups, e.g. carbonyl, cyano, chloro, and alkenic groups, with hydrogen is often difficult, because these sensitive functionalities are reduced faster with hydrogen than the nitro group.<sup>89</sup>”

The instant claims recite only an obvious variant of an old process. The replacement of catalytic hydrogenation or the noble metal/lewis acid mixture with group 8 transition metal carbonyl complexes with carbon monoxide reductants in the transformation of the nitro group was well established and favored.

### ***Conclusion***

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David K. O'Dell whose telephone number is (571)272-9071. The examiner can normally be reached on Mon-Fri 7:30 A.M.-5:00 P.M EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on (571)272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

D.K.O.

/Rita J. Desai/

Primary Examiner, Art Unit 1625